submitted to be in order in view of the Declaration evidence of record and the comments that follow.

This rejection appears to be based largely on a perceived lack of correlation between *in vitro* and animal model studies and *in vivo* results in patients. In an effort to advance this case, Applicants have made of record Declaration evidence that supports their position that targeting CD44 in mononuclear phagocytes inhibits HIV infection. In that regard, particular attention is directed to paragraphs 4 and 5 of the Weinhold Declaration which, it is earnestly believed, make clear the background against which the invention was made and the technical basis for Applicants' assertions regarding predictability *in vivo*, given the available data.

The invention described and claimed in the above application results from Applicants' finding that CD44 (the haluronate receptor) facilitates HIV infection in human cells. When CD44 is blocked by binding to an anti-CD44 antibody, there is a 40-80% reduction of HIV infection/expression in human monocytes *in vitro*. Applicants disclose in the application that the natural ligand of CD44, haluronate or haluronic acid, inhibits infection/expression up to 85%. In contrast, chondroitin sulfate, a polyanion that does not bind CD44, reportedly has little if any inhibitory activity.

The Examiner comments that it was well known that cellular CD4 is the predominant membrane protein that interacts with HIV. Applicants acknowledge in the application that *in vitro* studies had demonstrated that HIV infects human lymphocytes and mononuclear phagocytes by way of adherence of the virus gp120 to cellular membrane CD4. Applicants point out, however, that while anti-CD4 antibodies block HIV infection, this is usually not complete and that auxiliary cellular receptors for HIV had been postulated but not demonstrated. Declarant Weinhold states in his Declaration that Applicants' data indicate CD44 is one such auxiliary cellular receptor.

Declarant Weinhold goes on to say that the ability to block HIV infection of mononuclear phagocytes using CD44 blocking agents is of obvious significance. Mononuclear phagocytes are concentrated in the mucosa (for example, the vaginal mucosa) and thus are important target cells. Declarant Weinhold indicates that from a therapeutic standpoint, these target cells are readily accessible. That is, the CD44 blocking agent can be administered topically to the mucosal surface or, for example, within a condom. The application in fact makes specific reference to loco-regional (e.g., intravaginal) administration. Alternatively, the blocking agent can be administered parenterally.

Declarant Weinhold comments that the concept underlying the invention is a straightforward one and indicates that he sees little reason to doubt the effectiveness of the approach. Declarant Weinhold goes on in paragraphs (5) and (6) of his Declaration to provide basis for his view in this regard.

As regards the Examiner's comments at the top of page 4 of the Action, relating to Rivadeneira et al, clarification is requested. On their face, those comments are believed to miss the point of the present invention.

Finally, the Examiner is again reminded that a patent applicant enjoys the presumption that the invention can be practiced as claimed. The burden is on the examiner to provide evidence or reasoning inconsistent with the disclosure as to why such would not be the case. Respectfully, the broad brush assertions made by the Examiner here do not constitute such evidence or reasoning.

In view of the above comments, the Examiner is urged to reconsider his position. It is believed that having done so, the Examiner will find withdrawal of the rejection to be in order.

Claims 13-19 (it is believed 14-19 were intended) stand rejected under 35 USC 112, first paragraph. The rejection is traversed.

Claim 16, from which the remaining claims depend, is drawn to a method of inhibiting CD44-facilitated HIV infection of a mononuclear phagocyte. The claim

is not drawn to an agent that binds CD44 molecules present on the cell surface. As indicated above, it was Applicants that discovered, and disclose in the subject application, that CD44 facilitates HIV infection in humans. Given the nature of their contribution, it is entirely appropriate they be entitled to a method claim that covers the use of any and all agents that bind CD44 and in so doing block HIV infection. To require that Applicants' method claims be limited to any particular agent would be to unduly restrict Applicants in the scope of protection to which they are rightly entitled. Indeed, the Examiner's assertions to the contrary may be appropriate if it were the agent per se that was claimed. Since that is not the case here, the rejection is clearly in error and should be withdrawn.

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This application is submitted to be in condition for allowance and a Notice to the effect is requested.

Respectfully submitted,

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